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10/565,669	01/24/2006	Tomoharu Kiyuna	Q92767	2893

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EXAMINER	
CLOW, LORI A	

ART UNIT	PAPER NUMBER
1631	

NOTIFICATION DATE	DELIVERY MODE
05/24/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Advisory Action Before the Filing of an Appeal Brief	Application No.	Applicant(s)	
	10/565,669	KIYUNA ET AL.	
	Examiner	**Art Unit**	
	LORI A. CLOW	1631	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 05 May 2010 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.
   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *1-15,17 and 23-29*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

/Lori A. Clow/
Primary Examiner, Art Unit 1631

Continuation of 11. does NOT place the application in condition for allowance because: The rejections from the FINAL Office Action of 12/17/2009 are maintianed for the reasons of record and re-iterated below.

Claim Rejections - 35 USC § 101-Non-statutory Subject Matter
35 U.S.C. 101 reads as follows:
Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-15, 17, and 23-29 remain rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter, for the reasons set forth in the previous Office Action and re-iterated below.
Claims 1-15, 17, and 23-29 are drawn to a method of measuring a chromosome territory, the method detecting a difference in state between a plurality of cells containing a chromosome territory by measuring a desired area of said cells in information of a plurality of images comprising extracting data from images and classifying images into classes.
In accord with the decision in In re Bilski, a claim to a process or method must meet the machine-or-transformation test in order to be eligible under 35 USC 101 as statutory subject matter (In re Bilski, 545 F.3d 943, 88 USPQ2d 1385 (Federal Circuit, 2008). In other words, the prohibition on patenting abstract ideas has two distinct aspects: (1) when an abstract concept has no claimed practical application, it is not patentable; (2) while an abstract concept may have a practical application, a claim reciting an algorithm or abstract idea can state statutory subject matter only if it is embodied in, operates on, transforms, or otherwise is tied to another class of statutory subject matter under 35 U.S.C. §101 (i.e. a machine, manufacture, or composition of matter). (Gottschalk v. Benson, 409 U.S. 63, 175 USPQ 673, 1972), as clarified in In re Bilski, 545 F.3d 943, 88 USPQ2d 1385 (Federal Circuit, 2008) the test for a method claim is whether the claimed method is (1) tied to a particular machine or apparatus or (2) transforms a particular article to a different state or thing.
In the instant case, the method claims are not so tied to another statutory class of invention because the method steps that are critical to the invention are "not tied to any particular apparatus or machine" and therefore do not meet the machine-or-transformation test as set forth in In re Bilski 545 F.3d 943, 88 USPQ2d 1385 (Federal Circuit, 2008).

Response to Applicant's Arguments
1. Applicant states that they reapply the arguments from the Amendment dated September 24, 2009. Applicant also states that the "Examiner's assertion that Judge Michel's comments regarding the Bilski decision have "no bearing on the examination of process claims as decided by the CAFA and as directed by the instructions recited above" is illogical because Judge Michel authored the Bilski decision".
The Examiner respectfully disagrees with the characterization that In re Bilski does not apply to Applicant's invention. The Examiner directs Applicant to the Interim Examination Instructions for Evaluating Subject Matter Eligibility Under 35 USC 101 that can be found at http://www.uspto.gov/web/offices/pac/dapp/opla/2009-08 25_interim_101_instructions.pdf. The Examination Instructions clearly state that a claim to a process, of which is instantly claimed, must pass the machine-or-transformation test which ensures that the process is limited to a particular practical application. It is maintained that in the instant case, the method claims do not meet such requirement and therefore remain rejected.
Further, the Examiner is well aware that Judge Michel was a presiding Juge at the CAFC for the Bilski decision. However, the precedential decision, as rendered by the Bilski court, is reflected in the Guidelines recited above and follwed by the USPTO. The paper, to which Applicant's refer as being authored by Judge Michel, is an opinion paper and not a precedential court decision. The rejection is maintained.

Claim Rejections - 35 USC § 103
The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:
(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:
1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).
Claims 1-15, 17, and 23-29 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Parada et al. (Trends in Cell Biology (2002) Vol. 12, No. 9, pages 425-432; PTO form 1449 reference) in view of 7,136,540 (Kiyuna), for the reasons set forth in the previous Office Action and re-iterated below.
The instant claims are drawn to a method of measuring a chromosome territory, the method detecting a difference in state between a plurality of cells containing a chromosome territory by measuring a desired area in images having an attribute value. The method comprises extracting a chromosome territory from an image, standardizing and quantifying, detecting a difference in state

between cells and classifying said images into classes wherein classifying includes setting values for an attribute parameter indicating an attribute value of each of said classes and for a mixture ratio. Membership probabilities and evaluation functions are calculated to represent a goodness estimation based on said membership probability and a mixture probability distribution and classifying based on fitting or not fitting a predetermined condition.

In regard to claims 1, 5, and 11, Parada et al. teach that chromosomes occupy distinct territories in the interphase cell nucleus (abstract). Recent advances in microscopy allow the routine visualization of said chromosomes in the interphase nucleus and visualization of chromosome territories (see Section 1. Chromosome Territories; Figure 3). Parada et al. also teach that by observing chromosomal territories and positioning, functional roles may be elucidated (see section 5.). These observations in positioning also are extremely useful in areas of cancer detection and tissue specific arrangement of chromosomes, as is taught in Section 6.

Parada et al. do not teach the specifics of the statistical imaging techniques used in the microscopic analysis, however, Kiyuna does teach a method and system of picture region extraction in which a picture region is extracted based on class membership probability (abstract). Specifically, Kiyuna teaches the parameters of claims 1-15 and 17, as follows:

"first step in which the data space constituted by all the attribute values that may be taken by the each pixel on the picture is divided into subspaces with a given resolution, a collection of pixels, each of which takes an attribute value in the each subspace, the average of the attribute values of the pixels, and the number of the pixels are retained to constitute a coarse-grained space,

a second step in which the number of pixels in the each subspace is divided by the total number of pixels contained in the picture to calculate the coarse-grained empirical probability distribution in the coarse-grained data space,

a third step in which the class parameter, the number of the classes, and the mixture ratio of the classes, which define the attributes of the each class, are initialized,

a fourth step in which a conditional probability distribution under the class being specified is calculated from the class parameter that defines the attributes of the each class, and the conditional probability distribution under the class being specified is averaged within the each subspace to calculate a coarse-grained conditional probability distribution,

a fifth step in which a class membership probability, which is the probability that each pixel constituting the picture belongs to the each class, is calculated by multiplying the class mixture ratio by the coarse-grained conditional probability distribution,

a sixth step in which the class parameter and the class mixture ratio are updated so as to increase an evaluation function,

a seventh step in which a coarse-grained log-likelihood is calculated as the evaluation function using the coarse-grained conditional probability distribution,

an eighth step in which whether the evaluation function satisfies a given termination condition or not is examined, and

a ninth step in which after the evaluation function satisfies the given termination condition, the class parameter and the class mixture ratio are retained, and the region each pixel belongs to is determined based on the class membership probability to extract the desired region, the fourth, fifth, sixth, seventh and eighth steps being repeated until the evaluation function satisfies the given condition.

In the preferred construction, in the fourth step, when calculating the coarse-grained conditional probability distribution, the average value of the data included in the each subspace is calculated, and the average value is used to calculate the coarse-grained conditional probability distribution in the each subspace.

In another preferred construction, the picture region extraction method further comprises a tenth step in which whether the coarse-grained resolution is equal to the original resolution or not is examined when the evaluation function satisfies the given terminal condition in the eighth step, and an eleventh step in which the resolution of the subspace is reverted to the original resolution if the resolution of the coarse-graining is not the original resolution,

the fourth, fifth, sixth, seventh, and eighth steps being repeated until the given condition is satisfied, using the class parameter and the class mixture ratio that are retained in the ninth step as the initial value in the third step.

In another preferred construction, in the fourth step, when calculating the coarse-grained conditional probability distribution, the average value of the data included in the each subspace is calculated, and the average value is used to calculate the coarse-grained conditional probability distribution in the each subspace,

which comprises a tenth step in which whether the coarse-grained resolution is equal to the original resolution or not is examined when the evaluation function satisfies the given terminal condition in the eighth step, and an eleventh step in which the resolution of the subspace is reverted to the original resolution if the resolution of the coarse-graining is not the original resolution,

the fourth, fifth, sixth, seventh, and eighth steps being repeated until the given condition is satisfied, using the class parameter and the class mixture ratio that are retained in the ninth step as the initial value in the third step.

In another preferred construction, in the ninth step, the estimated class mixture ratio is multiplied by the total number of pixels constituting the picture to calculate the number of pixels belonging to the each class, and the pixels in decreasing order of the class membership probability are selected to determine the pixels belonging to the each class.

In another preferred construction, in the seventh step, AIC is used as the evaluation function, and the parameter is changed so that the evaluation function may be decreased in the sixth step.

In another preferred construction, in the seventh step, MDL is used as the evaluation function, and the parameter is changed so that the evaluation function may be decreased in the sixth step.

In another preferred construction, in the seventh step, Structural Risk is used as the evaluation function, and the parameter is changed so that the evaluation function may be decreased in the sixth step.

In another preferred construction, the third step comprises a first step in which a neighborhood radius which defines whether the each subspace is close to one another, and the number of the classes are set, a second step in which the representative value of each subspace is set for each sub-space, a third step in which the collection of the classification target subspace is set, a fourth step in which the subspace with the highest coarse-grained empirical probability is selected among the classification target subspaces, a fifth step in which all the subspaces having a representative value whose distance to the representative value of the subspace with the highest coarse-grained empirical probability falls within the neighborhood radius are selected as a neighborhood collection, a sixth step in which whether the shortest distance between the representative value of the subspace included in a class for which classification has already been completed, and the representative value of the subspace included in the neighborhood collection is larger than the neighborhood radius is examined, a seventh step in which the neighborhood collection is defined as a new class if the shortest distance between the representative value of the subspace included in a class for which classification has already been completed and the representative value of the subspace included in the neighborhood collection is larger than the neighborhood radius, the neighborhood collection is

deleted from the classification target subspace, and the fourth steps and later are repeated, an eighth step in which if the shortest distance is equal to or shorter than the neighborhood radius, the neighborhood collection is added to the classified classes, and the neighborhood collection is deleted from the classification target subspace, a ninth step in which whether the classification target subspace is an empty collection or not is examined, a tenth step in which if the classification target subspace is not an empty collection, the fourth step and later are repeated, and if the classification target subspace is an empty collection, whether the number of classes for which classification has already been completed is equal to a given number or more is examined, an eleventh step in which if the number of classes for which classification has already been completed is fewer than the given number, the neighborhood radius is diminished, and the third step and later are repeated, a twelfth step in which
if the classification target subspace is an empty collection and the number of classified classes is greater than a given number, the class parameter is calculated within each class and taken as the initial value of the class parameter, also, the ratio of the number of subspaces included in each class is taken as the initial value of the class mixture ratio.” (beginning column 1).

It would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to have used the imaging techniques of Kiyuna with the microscopic evaluation of chromosome territories, as taught by Parada et al. One would have had a reasonable expectation of success in doing so, as imaging statistical techniques are well know in the art for evaluation of cell and cellular structures and Parada et al. is a generalized method for extracting a target object region from image data.

Response to Applicant's Arguments
1. Applicant argues that "the major object of Kiyuna is to extract a cell region". Applicant argues that "to obtain relevant information, techniques not described in Kiyuna (e.g., setting a reference point for a distance calculation, standardizing the distance, standardizing the for of the cell) are needed".
This is not persuasive. Kiyuna clearly teaches statistical image manipulation, such as that which is perfromed in the instant claim set. Kiyuna teaches the distribution of space of pixels in regions of interest (which could be a regions of interest such as a chromosome territory). Kiyun clearly teaches ratio distributions and attribute parameters and classifying images into classes, as is outlined above and further taught at column 4.

No claims are allowed.